

### REMARKS

Entry of the amendments is respectfully requested. Claims 3-7, 9, 42-50, 52-54, 56, 58-64 have been amended. Claims 1, 2, 8, 10-41, 51, 55, and 57 have been canceled. Of the canceled claims, claims 1, 2, 30-40 are non-elected and had been withdrawn. Applicants reserve the right to file a divisional application on these non-elected claims. Claims 65-81 have been added. Claims 3-7, 9, 42-50, 52-54, 56, and 58-81 are pending in the application. Favorable reconsideration and allowance of this application is respectfully requested in light of the foregoing amendments and the remarks that follow.

#### 1. Interview Summary

The applicant thanks the Examiner for her helpful in-person interview, which was held on October 23, 2003. The substance of the Interview Summary is as follows. All of the claims were discussed and an agreement was not reached. Recommendations were made regarding declarations that distinguish over the art, and amendments to further define the invention regarding "effective amounts."

In addition, running analyses of the following strains was discussed: strain P63 (disclosed in U.S. Patent No. 6,455,063 to Rehberger, et al.), strain P5 (disclosed in U.S. Patent No. 6,120,810 to Rehberger, et al.), and strain Hh-GYOKI-1-123Sz (disclosed in U.S. Patent No. 5,139,777 to Ott, et al.) to determine whether these strains also (A) have a group I profile produced by *Xba* I digests of genomic DNA as shown in Figures 1-2 and

Table 3 of the instant application, as some of the proposed amended claims would require, and (B) have the following characteristics: (1) producing at least 0.9% (vol/vol) propionate in sodium lactate broth, and (2) producing at least 0.2% (vol/vol) propionate in rumen fluid (in vitro), as some of the proposed amended claims would require.

2. Amendments to the Specification

The specification has been amended on page 10 to add ATCC accession numbers. Table 3 on page 23 has been amended to eliminate the underlining of the word "acidipropionici" relating to Isolate Number 169. Finally, on page 30, the paragraph title "Glucose and Insulin" has been underlined.

3. Rejection Under §112, Second Paragraph

Claims 3-29 and 41-64 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The specifics are detailed immediately below.

a. The Rejection of Claims 3-9, 15-16, and 41-64

In particular, claims 3-9, 15-16, and 41-64 are rejected because allegedly the sole designation of the microorganism is by an internal strain number. Applicants wish to note for the record that claims 49 and 52-64 do not use the internal strain number. Therefore, claims 49 and 52-64 are not indefinite for use of an internal strain number.

Claims 4 and 49 have been amended herein to exclude specific strain numbers. Instead, these claims require that the microorganism has a group 1 profile produced by *Xba* I digests of genomic DNA as shown in Figures 1-2 and Table 3 of the instant application. Claims 3 and 50 as amended herein also do not recite specific strain numbers. Instead, these claims require that the microorganism has the following characteristics: (1) produce at least 0.9% (vol/vol) propionate in sodium lactate broth, and (2) produce at least 0.2% (vol/vol) propionate in rumen fluid (in vitro). The remaining claims (claims 5-9, 15, 16, 41-48, and 51-64) being rejected for containing internal strain numbers depend from one of claims 3, 4, 49, and 50 and do not contain specific strain internal numbers themselves. Claims 3-9, 15, 16, and 41-64 are therefore definite, as none of these claims recite a specific internal strain number.

In light of the amendments to claims 3, 4, 49, and 50, withdrawal of this rejection is respectfully requested.

New claims 65, 66, 68, 69, and 71 require strains having specific internal strain numbers (either P169 or P170). These claims are also believed to be definite, as for administrative convenience, the strains P169 and P170 were deposited at ATCC on June 18, 2003.

A Statement Under MPEP § 2406.06 is submitted herewith and is incorporated by reference herein. In the Statement, Marianne Bellot verifies that biological material was deposited at the ATCC under ATCC Accession Nos. ATCC PTA-5271 (P169) and

ATCC PTA-5272 (P170); that the biological material that was deposited under ATCC Accession Nos. ATCC PTA-5271 (P169) and ATCC PTA-5272 (P170) are biological materials specifically identified in the application (the filing date of which is relied upon) as filed; and that she is in a position to corroborate that the biological material which was deposited is a biological material specifically identified in the application (the filing date of which is relied upon) as filed because she personally made the deposit to the ATCC.

The applicant's representative hereby avers that the deposited materials have been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the materials so deposited will be irrevocably removed upon the granting of a patent.

b. The Rejection of Claims 10-29 and 46-48

Claims 10-29 and 46-48 stand rejected for having no claim step to ensure the benefit recited in the claim. Claims 10-29 have been canceled, obviating the rejection of these claims. Claims 46-48 have been amended to require testing of the relevant benefit before and after feeding the ruminant the microorganism and to require an improvement in that benefit.

Claim 46 requires "wherein during at least the first week of lactation, there is a statistically significant increase in the percent of protein in the milk produced by the

ruminant after the feeding of the microorganism when compared to a milk produced by the ruminant before it is fed the microorganism." Support for a statistically significant increase in the percent of protein in the milk can be found on page 29, lines 15-19 of the instant patent application.

Claim 47 requires "wherein the milk produced by the ruminant after the feeding of the microorganism has about 6% greater percent of fat for at least the first 12 weeks of lactation when compared to a milk produced by the ruminant before it is fed the microorganism." Support for this greater percent of fat in the percent of protein in the milk can be found on page 30, lines 3-6 of the instant patent application.

Claim 48 requires "wherein during the first week of lactation, the milk produced by the ruminant after the feeding of the microorganism has a statistically significant increase in solids-non-fat when compared to a milk produced by the ruminant before it is fed the microorganism." Support for statistically significant increases in the solids-non-fat in the milk can be found on page 29, line 20 to page 30, line 2 of the instant patent application.

In light of the cancellation of claims 10-29 and the amendments to claims 46-48, withdrawal of this rejection is respectfully requested.

c. The Rejection of Claims 14 and 15

Claims 14 and 15 stand rejected for the use of "comprises" in the claim. Claims 14 and 15 have been canceled, obviating the rejection of these claims. Withdrawal of the rejection of claims 14 and 15 is therefore requested.

The Examiner's suggestion of "microorganism is" has been incorporated into new claims 65, 66, 68, and 69.

d. The Rejection of Claims 10-29, 41-44, 46-48, 57-60, and 62-64

Claims 10-29, 41-44, 46-48, 57-60, and 62-64 stand rejected for using words of degree as a limitation. Claims 10-29, 41, and 57 have been canceled, obviating the rejection of these claims.

To address this rejection, claims 42-44, 46, 48, 58-60, 62, and 64 have been amended to insert "statistically significant" before the relevant term, e.g., claim 62 now requires a statistically significant increase in protein content. Additionally, claims 47 and 63 now require "about 6% higher percent of fat," as there was a trend found for this variable.

Support for these amendments can be found in the application as follows.

<u>Claims</u>	<u>Factor</u>	<u>Location of Support</u>
42, 58	energy balance	page 33, line 19-page 34, line 3
43, 59	plasma non-esterified fatty acids levels	page 32, line 17-page 33, line 2
44, 60	plasma leptin levels	page 33, lines 3-9
46, 62	percent protein	page 29, lines 15-19
47, 63	percent of fat	page 30, lines 3-6
48, 64	solids non-fat	page 29, line 20-page 30, line 2

To address the concern over using "a second ruminant" in various claims, this term has been replaced with references to a ruminant before it is fed the microorganism and the ruminant after it is fed the microorganism. This addresses the concern over whether the second ruminant would be a proper control.

The claims are also rejected for lack of an indication of the nature and amount of bacteria to be fed to achieve the results indicated. Claim 49 has been amended to require "feeding the ruminant an effective amount for colonization of the rumen of the ruminant of a microorganism" to address this rejection. Claim 3 has been similarly amended, although this claim was not specifically listed in the rejection.

In light of the cancellation of claims 10-29, 41, and 57 and the foregoing amendments, withdrawal of the rejection of claims 10-29, 41-44, 46-48, 57-60, and 62-64 is respectfully requested.

4. Rejection Under §112, First Paragraph

Claims 3-9, 15, and 41-64 stand rejected as not being enabled. Claims 8, 15, 41, 51, 55, and 57 were canceled, obviating the rejection of these claims. The rejection of the remaining claims is believed to have been obviated by appropriate amendments to the claims.

This rejection is believed to have been obviated in part by amending claims 3, 4, and 50 to delete references to internal strain numbers. The remaining claims depend from one of these claims and also do not reference internal strain numbers.

Independent claim 3 requires "feeding the ruminant an effective amount for colonization of the rumen of the ruminant of a microorganism of the genus *Propionibacterium*, which has the following characteristics: (1) producing at least 0.9% (vol/vol) propionate in sodium lactate broth, and (2) producing at least 0.2% (vol/vol) propionate in rumen fluid (in vitro)."

Independent claim 49 requires "feeding the ruminant an effective amount for colonization of the rumen of the ruminant of a microorganism of the genus



*Propionibacterium* having a group I profile produced by *Xba* I digests of genomic DNA as shown in Figures 1-2 and Table 3."

Claims 3 and 49 and the claims that depend therefrom are sufficiently enabled as of the filing of the instant patent application to allow one skilled in the art to make and use the invention without undue experimentation. As evidence of the enablement of these claims, applicants submit herewith a Rule 132 Declaration of inventor Thomas G. Rehberger. Dr. Rehberger's Declaration opens with a brief introductory statement of his familiarity with the application. He is a named inventor and is therefore intimately familiar with the subject matter of the application.

Paragraph 2 of the Declaration contains a brief biographical description of his employment and educational history. His complete *Curriculum vitae* is attached to the Declaration. Paragraph 2 of the Declaration concludes with Dr. Rehberger stating that he is one skilled in the art of the instant application.

At paragraph 8 of the Declaration, Dr. Rehberger cites portions of the patent application that show that the claims requiring the specific biochemical requirements of claim 3 are sufficiently enabled as of the filing date of the instant patent application to allow one skilled in the art to make and use the invention without undue experimentation. Therefore, claim 3 and the claims that depend therefrom were enabled at the time of the filing.

At paragraph 7 of Dr. Rehberger's Declaration, Dr. Rehberger cites portions of the patent application that show that claims requiring the specific DNA profile requirement of claim 49 are sufficiently enabled as of the filing date of the instant application.

In light of the amendments and the foregoing, withdrawal of the rejection of claims 3-9, 15, and 41-64 is respectfully requested.

5. Rejection of Claims 3-29 and 41-64 Based on the Prior Art

Claims 3-29 and 41-64 stand rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Rehberger et al. (U.S. Patent No. 6,455,063). In addition, claims 3-9 and 41-64 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Ott et al. (U.S. Patent No. 5,139,777).

The applicants respectfully traverse this rejection because, as is discussed below, neither the Rehberger et al. patent nor the Ott et al. patent discloses each and every element of the novel subject matter disclosed and set forth the claims. Therefore, reconsideration is in order and is respectfully requested.

Furthermore, the rejection of claims 3-29 and 41-64 as unpatentable over Rehberger et al. or Ott et al. is respectfully traversed, because, *inter alia*, there is no teaching or suggestion to combine or modify the references to produce the claimed invention. MPEP §2143.01.

a. The Rehberger et al. Patent

The Rehberger et al. patent discloses a propionibacteria strain P-63 for use in a direct fed microbial for animal feeds to reduce acidosis. Acidosis is a metabolic condition, characterized by an increase in hydrogen ion concentration that occurs when the body is no longer able to buffer free hydrogen ions in the blood. This usually causes the pH of the blood to drop (and become more acidic). Propionibacterium P-63 is a culture of the species *Propionibacterium jensenii*. (col. 4, lines 4-5). Strain P-63 was found to demonstrate superior anti-acidosis properties as compared to other lactate utilizing bacteria. (col. 4, lines 18-20). The P-63 strain was obtained from the Communicable Disease Laboratory in Atlanta, Georgia under the strain designation number PJ54. (col. 4, lines 4-7).

b. The Ott et al. Patent

The Ott et al. patent describes a composition and a method for improving the efficiency of ruminant feed utilization. In the Ott et al. patent, microorganisms were isolated from the rumen of sheep, as is detailed in Example 1 thereof. Isolated microorganisms were screened and several bacteria were assigned to the *Propionibacterium* genus. (col. 4, lines 59-63). Propionibacteria isolated by Ott et al.

included strains Hh-GYOKI-1-123Sz, and Hh-GYOKI-48a, which originated from Hh-GYOKI-1-123. (col. 4, lines 59-63).

c. §102 and §103 Rejections

Claims 8, 10-41, 51, 55, and 57 have been canceled, obviating the rejection of these claims.

The Examiner's attention is drawn to the above-referenced Rule 132 Declaration of inventor Thomas G. Rehberger, which provides further evidence of the differences between the strains recited in the claims and the strains disclosed in U.S. Patent No. 6,455,063 to Rehberger et al. (strain P63), and the Ott et al. patent, and U.S. Patent No. 6,120,180 to Rehberger (strain P5) (not cited against the claims, but discussed in the above-mentioned in-person interview of October 23, 2003).

At paragraph 3 of his Declaration, Dr. Rehberger states that the purpose of the Declaration is to present evidence demonstrating that the strains recited in the method claims of in the patent application are different from the strains disclosed in U.S. Patent No. 6,455,063 to Rehberger et al., U.S. Patent 6,120,810 to Rehberger et al., and U.S. Patent No. 5,139,777 to Ott et al.

At paragraph 4 of the Declaration, Dr. Rehberger describes the specific strains of the *Propionibacterium* genus that were tested: P63 (disclosed in U.S. Patent No.

6,455,063 to Rehberger et al.) and P5 (disclosed in U.S. Patent No. 6,120,810 to Rehberger et al.).

The strain Hh-GYOKI-1-123Sz (disclosed in U.S. Patent No. 5,139,777 to Ott et al., Accession No. NCAIM B (000287) of the National Collection of Agricultural and Industrial Microorganisms, Budapest, Hungary) was *not* tested due to its unavailability from the National Collection in Budapest. The details of the attempts made by Dr. Rehberger to obtain this strain are listed in paragraphs 4a-4e of the Rule 132 Declaration. Briefly, attempts to obtain the strain were made by telephone, email, and the web. However, it was not possible to obtain the strain.

Referring now to paragraph 4f of the Declaration, additional strains disclosed and deposited by Ott et al. in the '777 patent were not tested because neither of these strains are of the genus *Propionibacterium*: Hh-GYOKI-2-14Ab is of the *Veillonella* genus, (Ott, et al., col. 5, lines 6-7) and Hh-GYOKI-3-81Me is of the *Bifidobacteria* genus. (Ott, et al., col. 5, lines 17-19). One additional strain of the *Propionibacterium* genus is mentioned in the Ott, et al. patent: Hh-GYOKI-48a, which is said to originate from Hh-GYOKI-1-123. (Ott, et al. patent; col. 4, lines 61-63). However, this strain was not deposited at, and was not available from the National Collection in Budapest (see Exhibit C for list of strains that are available). Furthermore, the specifics on how Hh-GYOKI-48a was derived from Hh-GYOKI-1-123 are not disclosed in the Ott, et al. patent. Therefore, the Hh-GYOKI-48a strain was not tested.

i. The Rejection of Claim 3 and the Claims that Depend Therefrom:

Claim 3 has been amended to require feeding a ruminant an effective amount to colonize a rumen of the ruminant of a microorganism of the genus *Propionibacterium*, which has the following characteristics: (1) producing at least 0.9% (vol/vol) propionate in sodium lactate broth, and (2) producing at least 0.2% (vol/vol) propionate in rumen fluid (in vitro). To distinguish the invention of claim 3 over U.S. Patent No. 6,455,063 to Rehberger et al. (P63) and U.S. Patent No. 6,120,810 to Rehberger et al. (P5), Dr. Rehberger performed biochemical analyses of *Propionibacterium* strains P63, P5, and P169 (a representative strain having the above-listed biochemical requirements).

In paragraph 6 of his Declaration, Dr. Rehberger states that biochemical analysis of the propionate produced by the strains grown in sodium lactate broth was performed generally according to Example 1 of the patent application. However, in Example 1 of the patent application, the propionate levels were measured at 48 hours, whereas in the new materials, levels were measured at 24 and 72 hours. An increase in propionate levels would be expected over time, as can be seen by comparing the 24 levels to the 72 hour levels (see paragraph 6a of the Declaration).

Biochemical analysis of the (vol/vol) propionate produced in sodium lactate broth was performed on P63 and P5. The results are described in paragraph 6a of the Declaration and are shown in Exhibit F attached to the Declaration. As the results show,

neither strain P5 (disclosed the '810 patent to Rehberger et al.) nor strain P63 (disclosed in the '063 patent to Rehberger et al.) produce at least 0.9% (vol/vol) propionate in sodium lactate broth, as amended claim 3 requires.

Although tests of propionate production in rumen fluid are not shown, one skilled in the art would not expect the required level to be achieved by these strains because the sodium lactate broth is a far superior medium compared to rumen fluid (see Declaration, paragraph 6a).

In light of the amendment to claim 3; the above-detailed biochemical analysis of the P5 strain, disclosed in U.S. Patent No. 6,120,810 to Rehberger, et al., and P63 strain, disclosed in U.S. Patent No. 6,455,063 to Rehberger, et al.; and the lack of the availability of the strain Hh-GYOKI-1-123Sz disclosed in the Ott et al. patent, withdrawal of the rejection of claim 3, and the claims that depend therefrom, is requested.

ii. Rejection of Claim 49 and the Claims that Depend Therefrom:

Claim 49 has been amended to require a method of feeding a ruminant "an effective amount for colonization of the rumen of the ruminant of a microorganism of the genus *Propionibacterium* having a group I profile produced by *Xba* I digests of genomic DNA as shown in Figures 1-2 and Table 3." To distinguish the invention of claim 49 over U.S. Patent No. 6,455,063 to Rehberger et al. (P63) and U.S. Patent No. 6,120,810 to Rehberger et al. (P5), Dr. Rehberger performed pulsed-field gel electrophoresis

(PFGE) analysis of *Propionibacterium* strains P63, P5, and P169 (a representative strain having the above-listed biochemical requirements).

Beginning at paragraph 5 of his Rule 132 Declaration, Dr. Rehberger describes the pulsed-field gel electrophoresis (PFGE) analysis that was performed under his supervision. The PFGE analysis was performed on *Xba* I digested genomic DNA for strains P169, P63, and P5. These studies were performed according to the Materials and Methods described in paragraph 5a of the Declaration. These Materials and Methods were generally the same as those described at page 10, lines 7-10 and in Example 1 of the patent application, with the exception that some samples were grown in 2% glycine-supplemented sodium lactate broth, which weakens the cell wall of bacteria such that DNA can be more readily isolated.

Results of the PFGE analysis are discussed in paragraph 5c and are shown in Exhibit D of the Declaration. As the PFGE results show, neither strain P5 (disclosed in the '810 patent to Rehberger, et al.) nor strain P63 (disclosed in the '063 patent to Rehberger, et al.) have a group 1 profile produced by *Xba* I digests of genomic DNA as shown in Figures 1-2 and Table 3 of the patent application and as required by amended claim 49.

In addition to the PFGE analysis of strains P5, P63, P169, analysis using RAPD PCR of these strains was performed as outlined in paragraph 5b of the Declaration. Results of these RAPD PCR analyses are described in paragraph 5d and are shown in



Exhibit E of the Declaration. These results further show that strains P5 and P63 differ from P169, a representative strain having a group 1 profile.

In light of the amendment to claim 49; the above-detailed PFGE and RAPD PCR analyses of strains P5, P63, and P169; and the lack of the availability of the strain Hh-GYOKI-1-123Sz disclosed in the Ott et al. patent, withdrawal of the rejection of claim 49, and the claims that depend therefrom, is requested.

6. New Claims

New claims 65-81 have been added. Claims 65-67 depend from claim 3 and are believed to be in condition for allowance for at least the reasons that claim 3 is believed to be allowable. Claims 68-70 depend from claim 49 and are believed to be in condition for allowance for at least the reasons that claim 49 is believed to be allowable.

New independent claim 71 is narrower in scope than claim 3 in that it specifically requires strain P169. Claims 72-81 depend from claim 71. Claims 71-81 are believed to be in condition for allowance for at least the reasons that claim 3 is believed to be in condition for allowance.

CONCLUSION

It is submitted that original claims 3-7, 9, 42-50, 52-54, 56, and 58-64 are in compliance with 35 U.S.C. §§ 112, 102, and 103 and each defines patentable subject

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matter. New claims 65-81 are also believed to be in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Applicants request a three-month extension of time from November 18, 2003 to February 18, 2004 in which to respond to the Office Action dated August 18, 2003.

Enclosed is a check in the amount of \$860 in payment of the following fees by a small entity: 1) filing fee for a Request for Continued Examination (\$385), and 2) a three-month extension of time under 37 CFR 1.17(a)(3) (\$475). Authorization is given to charge any additional fees or credit any overpayment in connection with this or any future communication to Deposit Account No. 50-1170.

The Examiner is invited to contact the undersigned by telephone if it would help expedite matters.

Respectfully submitted,



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